# **Complete Summary**

## **GUIDELINE TITLE**

Atrial fibrillation: drug treatment and electric cardioversion.

## BIBLIOGRAPHIC SOURCE(S)

Finnish Medical Society Duodecim. Atrial fibrillation: drug treatment and electric cardioversion. In: EBM Guidelines. Evidence-Based Medicine [CD-ROM]. Helsinki, Finland: Duodecim Medical Publications Ltd.; 2004 Sep 14 [Various].

#### **GUIDELINE STATUS**

This is the current release of the guideline.

This guideline updates a previous version: Finnish Medical Society Duodecim. Atrial fibrillation: drug treatment and electric cardioversion. In: EBM Guidelines. Evidence-Based Medicine [CD-ROM]. Helsinki, Finland: Duodecim Medical Publications Ltd.; 2004 Mar 25 [Various].

## **COMPLETE SUMMARY CONTENT**

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# **SCOPE**

## DISEASE/CONDITION(S)

Atrial fibrillation and atrial flutter

**GUIDELINE CATEGORY** 

Treatment

CLINICAL SPECIALTY

Cardiology Family Practice Internal Medicine

## INTENDED USERS

Health Care Providers Physicians

# GUIDELINE OBJECTIVE(S)

Evidence-Based Medicine Guidelines collect, summarize, and update the core clinical knowledge essential in general practice. The guidelines also describe the scientific evidence underlying the given recommendations.

## TARGET POPULATION

Patients with atrial fibrillation or atrial flutter

#### INTERVENTIONS AND PRACTICES CONSIDERED

- 1. Direct current cardioversion
- 2. Drug therapy:
  - Digitalization (oral or intravenous digoxin)
  - Beta-blockers, such as metoprolol, atenolol, sotalol, esmolol, or bisoprolol
  - Calcium channel blockers, such as verapamil or diltiazem
  - Antiarrhythmics, such as flecainide, disopyramide, propafenone, quinidine, amiodarone, or intravenous ibutilide
  - Anticoagulants
- 3. Reduction or discontinuation of drugs that have negative chronotropic action
- 4. Pacemaker

## MAJOR OUTCOMES CONSIDERED

- Efficacy of treatment on the following:
  - Optimization of the ventricular rate
  - Restoration of sinus rhythm
  - Maintenance of sinus rhythm
- Mortality
- Adverse effects

# METHODOLOGY

## METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources) Hand-searches of Published Literature (Secondary Sources) Searches of Electronic Databases

## DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The evidence reviewed was collected from the Cochrane database of systematic reviews and the Database of Abstracts of Reviews of Effectiveness (DARE). In addition, the Cochrane Library and medical journals were searched specifically for original publications.

#### NUMBER OF SOURCE DOCUMENTS

Not stated

# METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

## RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

#### Levels of Evidence

- A. Strong research-based evidence. Multiple relevant, high-quality scientific studies with homogenic results.
- B. Moderate research-based evidence. At least one relevant, high-quality study or multiple adequate studies.
- C. Limited research-based evidence. At least one adequate scientific study.
- D. No research-based evidence. Expert panel evaluation of other information.

# METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses Systematic Review

## DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

# METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

#### RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

## **COST ANALYSIS**

A formal cost analysis was not performed and published cost analyses were not reviewed.

## METHOD OF GUIDELINE VALIDATION

## DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

## RECOMMENDATIONS

## MAJOR RECOMMENDATIONS

The levels of evidence [A-D] supporting the recommendations are defined at the end of the "Major Recommendations" field.

## **Principles**

- In acute atrial fibrillation (AF), a beta-blocker is used to control the heart rate.
- In chronic atrial fibrillation, or before an elective cardioversion, digoxin, a beta-blocker, verapamil, or diltiazem may be used: a ventricular rate of 60 to 80 beats per minute (bpm) is usually optimal. Do not give calcium channel blockers if the patient has cardiac insufficiency.
- The indications for, and timing of, electric cardioversion must be considered carefully.
- Acute AF (duration less than two days) can be treated with intravenous (i.v.)
  or oral flecainide if the patient does not have cardiac insufficiency,
  hypotension, or bradycardia and has not taken other drugs that block either
  the function of the sinus node or atrioventricular conduction.
- Electric cardioversion is indicated if the situation is urgent, if the patient has Wolff-Parkinson-White-syndrome, or is on medication that modifies the conduction system of the heart.

## **Digitalization**

- The patient with heart failure and acute AF is primarily digitalized, if electric cardioversion has not been planned, if the ventricular rate is >80 to 100 bpm, and if the patient has not used digitalis or has severe heart failure.
- Digitalization either intravenously or orally:
  - Initially, a slow intravenous injection of 0.25 mg digoxin. A dose of 0.125 mg is given at one-hour intervals, until the total dose is maximally 0.75 mg (three 0.25-mg ampoules).
  - In oral therapy, maintenance doses are usually administered, but if a more rapid action is needed, a loading dose of 0.75 to 1.0 mg of digoxin can be given.

## Optimizing the Ventricular Rate

- A rapid ventricular rate must be slowed down to attain an appropriate heart rate. A ventricular rate of 60 to 90 bpm is appropriate for most patients.
- The ventricular rate can be slowed down with an intravenous betablocker (e.g., metoprolol 5 mg, repeated twice at 5-min intervals and, in case of fast AF with stable haemodynamics, the total dose can be increased to up

- to 30 mg. Short-acting esmolol or 5 mg of verapamil are alternatives). If slowing the rate is not urgent, the drugs can be given orally (atenolol 25–50 mg x 1 or metoprolol 50–100 mg  $\times$  2, or verapamil 40 mg  $\times$  3) (Segal et al., 2000; DARE-20003312, 2002) [A].
- In cardiac insufficiency, verapamil and diltiazem may worsen heart failure. Therefore digoxin (Freestone, Kamath, & Lip, 2002) [A] is preferred. A beta-blocker can be used in small doses while carefully observing the response.
- If the ventricular response rate is slow and the patient is symptomatic, reduce the doses of drugs that have negative chronotropic action or stop the medication completely. If the patient continues to have bradycardia and symptoms, implanting a pacemaker should be considered.
- Digitalis optimizes the ventricular response rate during rest, and often digitalization is all that is needed in elderly patients. During exercise, however, the heart rate can increase too much, impairing exercise capacity. To prevent this, younger patients may need, instead of digitalis, a betablocker or a calcium channel blocker in exercise and mental stress as well as at rest.
- An increase in ventricular response rate in AF may be a sign of aggravated heart failure. In this case, merely slowing down the ventricular response rate is not sufficient.

## Restoration of Sinus Rhythm

- Measures to convert AF to sinus rhythm should be undertaken if the sinus rhythm has not been restored after the reduction of heart rate and correction of possible heart failure. However, in patients over 65 years of age, repeated cardioversion to maintain sinus rhythm does not improve survival or quality of life compared to rate control of AF (Golzari, Cebul, & Bahler, 1996; DARE-968388, 1999; Van Gelder et al., 2002; Wyse et al., 2002) [B].
- Electric cardioversion is recommended if the patient
  - Has used several antiarrhythmic drugs
  - Is hypotensive
  - Is in a critical condition because of the arrhythmia
  - Has chronic AF
- Drugs used in this indication include flecainide and propafenone; previously, quinidine 0.2 g 3 times at 2-hour intervals was often used in some countries.
   Monitoring the patient during the conversion of the rhythm, and for at least 3 hours after it, is recommended because of the risk of ventricular tachycardia.

# Conversion of the Rhythm with Flecainide

- Note the following contraindications
  - Dysfunction of the sinus node should be considered if acute AF with ventricular rate <80 bpm when the patient has not taken any medication that slows the ventricular response rate.
  - Second- or third-degree atrioventricular (AV) block
  - Severe cardiac insufficiency
  - Use of a class I antiarrhythmic drug or sotalol more than 160 mg/day, or less than 8 hours since the ingestion of the last sotalol tablet. If the patient is not in a hospital with special care facilities, it may be advisable not to use pharmacological cardioversion in patients on antiarrhythmic medication.

- Mix flecainide in 100 mL of 5% glucose. The dose is 2 mg/kg, maximally 150 mg as an infusion over 30 minutes. Discontinue the infusion if the sinus rhythm is restored.
- Monitor the patient for at least one hour after the restoration of the sinus rhythm; after that the patient is allowed to stand up. The patient may not leave the premises during the first three hours after restoration of the rhythm.
- If sinus rhythm has not been restored in three hours, perform electric cardioversion.

## Treatment of Atrial Flutter

- Electric cardioversion is the optimal treatment.
- Verapamil and digoxin slow the ventricular response rate.
- With sufficient digitalization, the rhythm usually reverts to atrial fibrillation, which is better tolerated than an atrial flutter.
- Intravenous ibutilide restores sinus rhythm in 60% of patients who have had AF or flutter for less than 30 days. The patient should be monitored for a few hours because of the risk of proarrhythmia (about 2%).

# Maintenance of Sinus Rhythm

- Rule out hyperthyroidism as the cause of AF.
- Digoxin does not prevent the recurrence of AF. However, in heart failure digoxin prevents the recurrence of supraventricular arrhythmia.
- Sodium channel blockers (quinidine, disopyramide, flecainide, and propafenone) must not be used if the left ventricular ejection fraction is below 40% (e.g., after myocardial infarction), because they increase the likelihood of serious proarrhythmia. If therapy with sodium channel blockers is initiated, left ventricular function must be estimated. The therapy should be initiated in a hospital, unless arrhythmia is primary and not caused by cardiac pathology.
- Beta-blockers (metoprolol 50–100 mg x 1 [Kuhlkamp et al., 2000] [B], bisoprolol 5 mg x 1, and sotalol 80–160 mg x 2) prevent recurrence of AF and are especially suitable for patients with ischaemic heart disease or high blood pressure. Heart failure does not prevent the use of beta blockers but is an indication for it. The treatment should be started cautiously with a small dosage. Because sotalol lengthens the QT interval, it is being discarded. (Southworth et al., 1999; DARE-991282, 2001) [C].
- Beta-blockers are suitable for the prevention of arrhythmias associated with physical exercise.
- Flecainide (Zarembski et al., 1995; DARE-988075, 1999) [C], propafenone (Reimold, Maisel, & Antman, 1998; DARE-981970, 2000) [A], and amiodarone (Zarembski et al., 1995; DARE-988075, 1999) [C] are effective in preventing atrial fibrillation, but the therapy should be initiated only after consultation of a specialist in internal medicine or cardiology. These antiarrhythmic agents are often combined with a selective beta-blocker. Amiodarone is also used as a short-course prophylactic medication in association with surgical procedures.

## Anticoagulant Therapy After Conversion

- Anticoagulation is usually continued for 4 weeks after the conversion of the rhythm. Embolic risk is high after restoration of sinus rhythm (e.g., in patients with hyperthyroidism). The mechanical function of the atria begins slowly, and formation of thrombi may continue even during electrical sinus rhythm. Continuation of anticoagulation also offers the possibility of repeating electric cardioversion during the follow-up visit, if the fibrillation has recurred. This is possible in patients who have not started a prophylactic medication after the first electric cardioversion.
- See related EBM guideline on Indications and Contraindications of Anticoagulant Therapy.

# Consultation About Prophylactic Treatment

Prophylaxis of AF with antiarrhythmic drugs requires knowledge of cardiology, as sodium channel blockers (e.g., quinidine, disopyramide, flecainide, propafenone) may be a greater risk to the cardiac patient than AF as such.

# Related Evidence

- Digoxin does not return atrial fibrillation into normal rhythm any more efficiently than placebo (Freestone, Kamath, & Lip, 2002) [B].
- Low-dose amiodarone (mean amiodarone dose per day ranged from 152–330 mg) has thyroid, neurologic, dermatologic, ocular, and bradycardic adverse effects (Vorperian et al., 1997; DARE-971109, 1999; Hohnloser, Klingenheben, & Singh, 1994; DARE-948059, 1999) [A].
- Ablation and pacing therapy significantly reduce cardiac symptoms and health care use in patients with refractory atrial fibrillation and tachyarrhythmia (Wood et al., 2000; DARE-20000672, 2002) [A].
- Pharmacological therapies or pacing appear to be favourable interventions for prevention of atrial fibrillation after cardiac surgery (Crystal et al., 2004) [B].

## Definitions:

## Levels of Evidence

- A. Strong research-based evidence. Multiple relevant, high-quality scientific studies with homogenic results.
- B. Moderate research-based evidence. At least one relevant, high-quality study or multiple adequate studies.
- C. Limited research-based evidence. At least one adequate scientific study.
- D. No research-based evidence. Expert panel evaluation of other information.

## CLINICAL ALGORITHM(S)

None provided

# EVIDENCE SUPPORTING THE RECOMMENDATIONS

## REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

## TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Concise summaries of scientific evidence attached to the individual guidelines are the unique feature of the Evidence-Based Medicine Guidelines. The evidence summaries allow the clinician to judge how well-founded the treatment recommendations are. The type of supporting evidence is identified and graded for select recommendations (see the "Major Recommendations" field).

# BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

#### POTENTIAL BENEFITS

Appropriate treatment for the optimization of ventricular rate and restoration and maintenance of sinus rhythm

## POTENTIAL HARMS

- Low-dose amiodarone (400 mg/day) has thyroid, neurologic, dermatologic, ocular, and bradycardic adverse effects. Amiodarone appears to be associated with a low incidence of proarrhythmic events with torsade de pointes developing in less than 1% of cases.
- Both sotalol and quinidine tend to increase mortality with long-term therapy.

## CONTRAINDICATIONS

## **CONTRAINDICATIONS**

- Calcium channel blockers (diltiazem, verapamil) are contraindicated in patients with cardiac insufficiency.
- Flecainide is contraindicated:
  - In patients with dysfunction of the sinus node: acute atrial fibrillation with ventricular rate <80 beats per minute (bpm) when the patient has taken no medication that slows the ventricular response rate
  - In patients with second- or third-degree atrioventricular block
  - In patients with severe cardiac insufficiency
  - With the use of class I antiarrhythmic drug, sotalol, more than 160 mg/day, or less than 8 hours since ingestion of the last sotalol tablet. If the patient is not in a hospital with special care facilities, it may be advisable not to use pharmacotherapy in patients on antiarrhythmic medication.

# IMPLEMENTATION OF THE GUIDELINE

## DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

# INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

**IOM CARE NEED** 

Getting Better Living with Illness

IOM DOMAIN

Effectiveness

## IDENTIFYING INFORMATION AND AVAILABILITY

## BIBLIOGRAPHIC SOURCE(S)

Finnish Medical Society Duodecim. Atrial fibrillation: drug treatment and electric cardioversion. In: EBM Guidelines. Evidence-Based Medicine [CD-ROM]. Helsinki, Finland: Duodecim Medical Publications Ltd.; 2004 Sep 14 [Various].

**ADAPTATION** 

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2001 Apr 30 (revised 2004 Sept 14)

GUIDELINE DEVELOPER(S)

Finnish Medical Society Duodecim - Professional Association

SOURCE(S) OF FUNDING

Finnish Medical Society Duodecim

**GUI DELI NE COMMITTEE** 

Editorial Team of EBM Guidelines

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Primary Author: Editors

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

**GUIDELINE STATUS** 

This is the current release of the guideline.

This guideline updates a previous version: Finnish Medical Society Duodecim. Atrial fibrillation: drug treatment and electric cardioversion. In: EBM Guidelines. Evidence-Based Medicine [CD-ROM]. Helsinki, Finland: Duodecim Medical Publications Ltd.; 2004 Mar 25 [Various].

## GUIDELINE AVAILABILITY

This guideline is included in a CD-ROM titled "EBM Guidelines. Evidence-Based Medicine" available from Duodecim Medical Publications, Ltd, PO Box 713, 00101 Helsinki, Finland; e-mail: <a href="mailto:info@ebm-guidelines.com">info@ebm-guidelines.com</a>; Web site: <a href="mailto:www.ebm-guidelines.com">www.ebm-guidelines.com</a>.

#### AVAILABILITY OF COMPANION DOCUMENTS

None available

## PATIENT RESOURCES

None available

## NGC STATUS

This summary was completed by ECRI on August 28, 2001. The information was verified by the guideline developer as of October 26, 2001. This summary was updated by ECRI on December 9, 2002. This summary was verified by the developer on April 2, 2003. This summary was updated again by ECRI on March 29, 2004, September 30, 2004, and most recently on February 18, 2005.

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